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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:
Marie-Odile Galcera Contour, et al.
Serial No.: 10/562,949
Filed: February 10, 2006
For: BENZOTHIAZOLE.. PROCESSES

: Group: 1626
: Examiner: Cheng, Karen

Hedman and Costigan
1185 Avenue of the Americas
New York, NY 10036
August 28, 2007

SUPPLEMENTAL RESPONSE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Supplemental to the amendment of July 20, 2007, Applicants are submitting herewith a sworn English translation of French priority Serial No. 03 07648 filed June 25, 2003 which removes the Galcera Contour et al. reference which has a publication date of July 10, 2003.

Therefore, it is believed that the application is now in condition for allowance and favorable reconsideration of the application is requested.

Respectfully submitted,
Hedman and Costigan

Charles A. Muserlian #19,683
Attorney for Applicants
Tel. 212 302 8989

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Enclosures

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Marie-Louise Pinsel

Marie-Louise Pinsel

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF TRANSLATION

Honourable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

I, JOHN CHARLES McGILLEY, B.A. M.I.T.I., Technical Translator, of c/o Priory Translations Limited, 11, Magdalen Street, Colchester, Essex, England,

hereby state:

THAT I am well acquainted with the French and English languages.

THAT I translated the document identified as French Patent Application No. 03 07648 filed at the National Institute of Industrial Property on 25th June 2003, from French into English;

THAT the attached English translation is a true and correct translation of French Patent Application No. 03 07648 .

to the best of my knowledge and belief; and

THAT all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true and further, that these statements are made with the knowledge that wilful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code

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Patent of invention

Utility certificate

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Drawn up in Paris, 20th July 2007

For the Director General
of the National Institute
of Industrial Property
The Head of the Patent Department

Martine PLANCHE

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PATENT OF INVENTION
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Delivery of documents Date **25th June 2003** Place **75 INPI Paris** National Registration No. **0307648** assigned by INPI Date of filing assigned by INPI **25th June 2003**	**1.Name and address of applicant or representative to whom correspondence should be addressed** Monsieur André BOURGOUIN BEAUFOUR IPSEN - S.C.R.A.S. Direction de la Propriété Industrielle 24 rue Erlanger 75781 PARIS CEDEX 16
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2. NATURE OF APPLICATION	**Tick one of the following 4 boxes**
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Application for utility certificate	☐
Divisional application *Initial patent application* *or initial application for utility certificate*	☐ No. Date / / No. Date / /
Conversion of a European patent application *Initial patent application*	☐ No. Date / /

3. TITLE OF INVENTION (200 characters or spaces maximum)
Benzothiazole-4,7-diones and benzooxazole-4,7-diones substituted in position 5 or 6 and processes for their preparation

4. DECLARATION OF PRIORITY OR REQUEST FOR BENEFIT FROM THE FILING DATE OF A PREVIOUS FRENCH APPLICATION	Country or organisation Date: / / No. Country or organisation Date: / / No. Country or organisation Date: / / No. ☐ **If there are other priorities, tick the box and use the printed form "Continuation"**
5. APPLICANT	☐ **If there are other applicants, tick the box and use the printed form "Continuation"**
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First names	
Legal form	Simplified joint stock company
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APE-NAF code	741J
Address – Street	42 rue du Docteur Blanche
Address – Post code and town	75016 PARIS
Country	FRANCE
Nationality	French
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PATENT OF INVENTION
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6. REPRESENTATIVE		
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The inventors are the applicants		☐ Yes ☒ No **In this case, supply a separate designation of inventor(s)**
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9. REDUCTION IN LEVEL OF FEES		**Only for natural persons** ☐ Requested for the first time for this invention (*attach a notice of no charge)* ☐ Requested prior to this filing (*attach a copy of the decision of acceptance for this invention or indicate its reference no.):*
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10. SIGNATURE OF APPLICANT OR REPRESENTATIVE: **(name and capacity of signatory)** André BOURGOUIN, Representative		**STAMP OF PREFECTURE OR INPI** Mme BLANCANEAUX

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Benzothiazole-4,7-diones and benzooxazole-4,7-diones substituted in position 5 or 6 and their preparation processes

A subject of the present invention is certain derivatives of benzothiazole-4,7-diones and benzooxazole-4,7-diones substituted in position 5 or in position 6, which inhibit the Cdc25 phosphatases, in particular the Cdc25-C phosphatase, and/or the CD45 phosphatase as well as a process for the preparation of such derivatives and of the synthesis intermediates useful in the implementation of this process.

Control of the transition between the different phases of the cell cycle during mitosis or meiosis is ensured by a group of proteins the enzyme activities of which are associated with different states of phosphorylation. These states are controlled by two large classes of enzymes: the kinases and the phosphatases.

Synchronization of the different phases of the cell cycle thus allows reorganization of the cell architecture at each cycle in the whole of the living world (microorganisms, yeasts, vertebrates, plants). Among the kinases, the cyclin-dependent kinases (CDKs) play a major role in this control of the cell cycle. The enzyme activity of these different CDKs is controlled by two other families of enzymes which work in opposition (Jessus and Ozon, *Prog. Cell Cycle Res.* (1995), **1**, 215-228). The first includes kinases such as Wee1 and Mik1 which deactivate the CDKs by phosphorylating certain amino acids (Den Haese et al., *Mol. Biol. Cell* (1995), **6**, 371-385). The second includes phosphatases such as Cdc25 which activate the CDKs by dephosphorylating tyrosine and threonine residues of CDKs (Gould et al., *Science* (1990), **250**, 1573-1576).

The phosphatases are classified in 3 groups: the serine/threonine phosphatases (PPases), the tyrosine phosphatases (PTPases) and the dual-specificity phosphatases (DSPases). These phosphatases play an important role in the regulation of numerous cell functions.

As regards human Cdc25 phosphatases, 3 genes (Cdc25-A, Cdc25-B and Cdc25-C) code for the Cdc25 proteins. Moreover, variants originating from alternative splicing of the Cdc25B gene have been identified (cf. for example Baldin et al., *Oncogene* (1997), **14**, 2485-2495).

The role of the Cdc25 phosphatases in oncogenesis is now better known and the action mechanisms of these phosphatases are illustrated in particular in the following

references: Galaktionov et al., *Science* (1995), **269**, 1575-1577; Galaktionov et al., *Nature* (1996), **382**, 511-517; and Mailand et al., *Science* (2000), **288**, 1425-1429.

In particular, the overexpression of the different forms of Cdc25 is now reported in numerous series of human tumors:

- Breast cancer: cf. Cangi et al., *Résumé 2984, AACR meeting San Francisco*, 2000);

- Lymphomas: cf. Hernandez et al., *Int. J. Cancer* (2000), **89**, 148-152 and Hernandez et al., *Cancer Res.* (1998), **58**, 1762-1767;

- Cancers of the neck and head: cf. Gasparotto et al., *Cancer Res.* (1997), **57**, 2366-2368.

Moreover, E. Sausville's group reports an inverse correlation between the level of expression of Cdc25-B in a panel of 60 lines and their sensitivities to CDK inhibitors, suggesting that the presence of Cdc25 can bring a resistance to certain antineoplastic agents and more particularly to CDK inhibitors (Hose et al., *Proceedings of AACR, Abstract* 3571, San Francisco, 2000).

Among other targets, the pharmaceutical industry is therefore at present researching compounds capable of inhibiting the Cdc25 phosphatases in order to use them in particular as anti-cancer agents.

The Cdc25 phosphatases also play a role in neurodegenerative diseases such as Alzheimer's disease (cf. Zhou et al., *Cell Mol. Life Sci.* (1999), **56**(9-10), 788-806; Ding et al., *Am. J. Pathol.* (2000), **157**(6), 1983-90; Vincent et al., *Neuroscience* (2001), **105**(3), 639-50) in such a manner that it is also possible to envisage using compounds possessing an inhibition activity on these phosphatases in order to treat these diseases.

Another problem addressed by the invention is research into medicaments intended to prevent or treat the rejection of organ transplants or also to treat auto-immune diseases. In these disorders/diseases, the non-appropriate activation of lymphocytes and monocytes/macrophages is involved. The immunosuppressive medicaments known at present have side effects which could be diminished or modified by products specifically targeting the signalling pathways in hematopoietic cells which initiate and maintain inflammation.

The CD45 phosphatase plays a crucial role in the transmission of signals from receptors on the T lymphocytes by regulating the phosphorylation and the activity of the tyrosine

kinases of the src family, the negative regulation sites $p56^{lck}$ and $p59^{fyn}$ of which it is capable of dephosphorylating.

The CD45 phosphatase is therefore a potential target in the treatment of immune diseases. In fact, the blocking of the CD45 phosphatase by an anti-CD45 antibody inhibits the activation of the T lymphocytes *in vitro* (Prickett and Hart, *Immunology* (1990), **69**, 250-256). Similarly, the T lymphocytes of transgenic mice not expressing CD45 (CD45 *knock-out mice*) do not respond to stimulation by an antigen (Trowbridge and Thomas, *Annu. Rev. Immunol.* (1994), **12**, 85-116).

Moreover, CD45 would be capable of dephosphorylating a sub-unit associated with Lyn, which would trigger a flow of calcium and activation of the mastocytes. Hamaguchi et al. (*Bioorg. Med. Chem. Lett.* (2000), **10,** 2657-2660) have shown that a particular CD45 inhibitor (with an IC_{50} equal to 280 nM) would suppress the release of histamine from rat peritoneal mastocytes and would protect mice from anaphylactic shock.

The advantage of finding CD45 phosphatase inhibitors would therefore appear obvious in particular when there is interest in:

- obtaining an immunosuppressive effect in general, and in particular:
    - within the scope of the treatment of auto-immune diseases (Zong et al., *J. Mol. Med.* (1998), **76**(8), 572-580) such as for example multiple sclerosis or autoimmune encephalitis (Yacyshyn et al., *Dig. Dis. Sci.* (1996), **41**(12), 2493-8) and diabetes (Shimada et al., *J. Autoimmun.* (1996), **9**(2), 263-269);
    - within the scope of the treatment of transplant rejections;
- in the treatment of inflammation in general, and in particular:
    - within the scope of the treatment of arthritis (Pelegri et al., *Clin. Exp. Immunol.* (2001), **125**(3), 470-477), rheumatoid arthritis, rheumatic diseases, conjunctivitis (Iwamoto et al., *Graefes Arch. Clin. Opthalmol.* (1999), **237**(5), 407-414) and pruritic diseases;
    - within the scope of the treatment of digestive inflammatory diseases such as for example Crohn's disease (Yacyshyn et al., *Dig. Dis. Sci.* (1996), **41**(12), 2493-2498), haemorrhagic rectocolitis and hepatitis (Volpes et al., *Hepatology* (1991), **13**(5), 826-829); and

- in the treatment of allergies (Pawlik et al., *Tohoku J. Exp. Med.* (1997), **182**(1), 1-8).

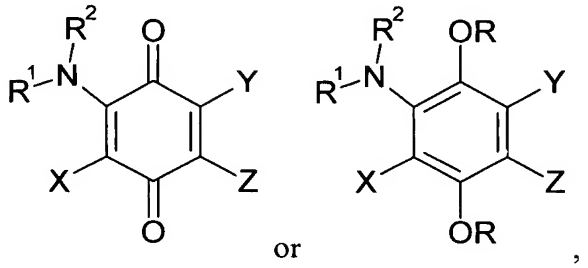
The invention offers novel Cdc25 phosphatase inhibitors (in particular Cdc25-C phosphatase inhibitors), and/or CD45 phosphatase inhibitors, which are derivatives of benzothiazole-4,7-diones and benzooxazole-4,7-diones corresponding to the general formula **(I)** defined hereafter. Given the above, these compounds are capable of being used as medicaments, in particular in the treatment of the following diseases/disorders:

- inhibition of tumorous proliferation alone or in combination with other treatments;
- inhibition of normal cell proliferation alone or in combination with other treatments;
- neurodegenerative diseases such as Alzheimer's disease;
- prevention of spontaneous alopecia;
- prevention of alopecia induced by exogenous products;
- prevention of radiation-induced alopecia;
- prevention of spontaneous or induced apoptosis of normal cells;
- prevention of meiosis and fertilization;
- prevention of the maturation of oocytes;
- all the diseases/all the disorders corresponding to uses reported for CDK inhibitors, and in particular non-tumorous proliferative diseases (for example: angiogenesis, psoriasis or restenosis), tumorous proliferative diseases, parasitology (proliferation of protozoans), viral infections, neurodegenerative diseases, myopathies;
- all the diseases/all the disorders corresponding to clinical uses of vitamin K and its derivatives;
- autoimmune diseases such as for example multiple sclerosis and rheumatoid arthritis; and
- diabetes.

Moreover, the compounds of the present invention are also, due to their Cdc25 phosphatase inhibition properties, capable of being used to inhibit the proliferation of microorganisms, in particular yeasts. One of the advantages of these compounds is their low toxicity on healthy cells.

A certain number of derivatives of benzothiazole-4,7-diones and benzooxazole-4,7-diones are already known.

In particular, the patent GB 1 534 275 relates to herbicides, the active ingredient of which is a compound corresponding to one of the general formulae



or

(A1) or **(A2)**

in which:

R^1 represents in particular a hydrogen atom or an alkyl or cycloalkyl radical;

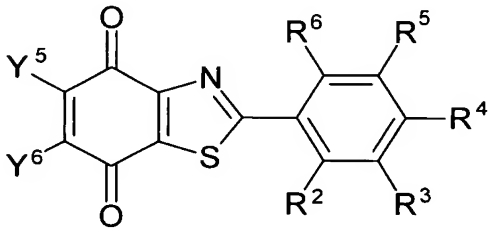
R^2 represents in particular a hydrogen atom, an alkyl or cycloalkyl radical;

X represents in particular a halogen atom or an alkoxy radical;

Y and Z can in particular represent together with the carbon atoms which carry them a thiazole ring optionally substituted by an alkyl radical; and

R represents in particular an alkyl radical.

Moreover, the Patent Application PCT WO 99/32115 described the compounds of general formula **(A3)**



(A3)

in which:

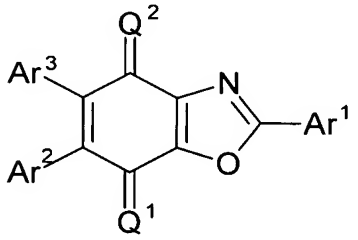
the substituents R^2-R^6 are chosen from the group constituted by a hydrogen atom, electron-donating substituents, electron-attracting substituents and electron-modulating substituents;

and Y^5 and Y^6 are in particular chosen from the group constituted by a hydrogen atom, electron-donating substituents, electron-attracting substituents and electron-modulating substituents.

In the Patent Application PCT WO 99/32115, the term "electron-donating substituent" refers to a functional group having a tendency to donate electronic density; the substituents alkyl, alkenyl and alkynyl are mentioned. Throughout this Patent Application, "electron-attracting substituent" refers to a functional group having a tendency to attract electronic density; the substituents cyano, acyl, carbonyl, fluoro, nitro, sulphonyl and trihalomethyl are mentioned. Finally, an "electron-modulating substituent" is defined in this Application as a functional group having a tendency to modulate the electronic density, which can both attract and donate electrons and is therefore such that it can stabilize a cationic intermediate in an aromatic electrophilic substitution reaction; a functional group including, for example, amino substituents (for example $-NH_2$, alkylamino or dialkylamino), hydroxy, alkoxy or aryl, heterocyclic substituents, halogen atoms, etc. are mentioned.

The compounds of general formula **(A3)** are presented as modulators of the ryanodine receptors which can be used as pesticides or as therapeutic agents, for example in the treatment of congestive cardiac failure, migraine headaches, hypertension, Parkinson's disease or Alzheimer's disease or in the prevention of miscarriage.

Finally, the derivatives of benzooxazole-4,7-diones of general formula **(A4)**



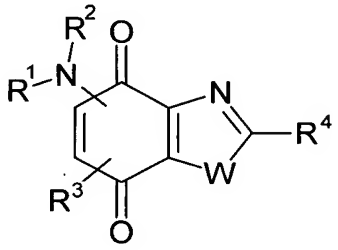
(A4)

in which:

Ar^1 represents an optionally substituted aryl radical,
each of Ar^2 and Ar^3 represents a hydrogen atom or an optionally substituted aryl radical, and
each of Q^1 and Q^2 represents in particular O,

are described as active constituents of photosensitive layers of photoreceptors.

In the Patent Application PCT/FR02/04544, the Applicant has described the compounds corresponding to general formula **(I)**



(I)

in which:

R^1 represents a hydrogen atom or an alkyl, alkoxyalkyl, alkylthioalkyl, cycloalkyl, $-(CH_2)-X-Y$, $-(CH_2)-Z-NR^5R^6$ radical or a $-CHR^{35}R^{36}$ radical in which R^{35} and R^{36} form together with the carbon atom which carries them an indanyl or tetralinyl radical, or also R^{35} and R^{36} form together with the carbon atom which carries them a saturated heterocycle containing 5 to 7 members and 1 to 2 heteroatoms chosen from O, N and S, the nitrogen atoms of said heterocycle being optionally substituted by radicals chosen from the alkyl radicals and the benzyl radical,

R^1 also being able, when W represents O, to represent moreover a carbocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl or alkoxy radical,

X representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

Y representing a saturated carbon-containing cyclic system containing 1 to 3 condensed rings chosen independently from rings with 3 to 7 members, or Y representing a saturated heterocycle containing 1 to 2 heteroatoms chosen independently from O, N and S and attached to the X radical by an N or CH member, said saturated heterocycle moreover containing 2 to 6 additional members chosen independently from $-CHR^7-$, $-CO-$, $-NR^8-$, $-O-$ and $-S-$, R^7 representing a hydrogen atom or an alkyl radical and R^8 representing a hydrogen atom or an alkyl or aralkyl radical, or also Y representing a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^9 and an $NR^{10}R^{11}$ radical, R^9 representing a hydrogen atom or an alkyl or phenyl radical, and R^{10} and R^{11} independently representing alkyl radicals,

Z representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

R^5 and R^6 being chosen independently from a hydrogen atom, an alkyl, aralkyl or $-(CH_2)_n-OH$ radical in which n represents an integer from 1 to 6,

or R^5 representing an alkoxycarbonyl, haloalkoxycarbonyl or aralkoxycarbonyl radical and R^6 representing a hydrogen atom or a methyl radical,

or also R^5 and R^6 forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{12}R^{13}-$, -O-, -S- and $-NR^{14}-$ radicals, R^{12} and R^{13} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{14} representing a hydrogen atom or an alkyl or aralkyl radical, or also R^{14} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^2 representing a hydrogen atom or an alkyl or aralkyl radical;

or also R^1 and R^2 forming together with the nitrogen atom a heterocycle with 4 to 8 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{15}R^{16}-$, -O-, -S- and $-NR^{17}-$ radicals, R^{15} and R^{16} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{17} representing a hydrogen atom or an alkyl or aralkyl radical;

R^3 represents a hydrogen atom, a halogen atom, or an alkyl, haloalkyl, alkoxy or alkylthio radical;

R^4 represents an alkyl, cycloalkyl, cycloalkylalkyl, cyano, amino, $-CH_2-COOR^{18}$, $-CH_2-CO-NR^{19}R^{20}$ or $-CH_2-NR^{21}R^{22}$ radical, or R^4 represents a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy, haloalkoxy or $NR^{37}R^{38}$ radical, or also R^4 represents a phenyl radical possessing two substituents which form together a methylenedioxy or ethylenedioxy radical,

R^{18} representing a hydrogen atom or an alkyl radical,

R^{19} representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^{23} radical and an $NR^{24}R^{25}$ radical, R^{23} representing a

hydrogen atom or an alkyl or phenyl radical, and R^{24} and R^{25} independently representing alkyl radicals,

R^{20} representing a hydrogen atom or an alkyl radical,

or also R^{19} and R^{20} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{26}R^{27}-$, -O-, -S- and $-NR^{28}-$ radicals, R^{26} and R^{27} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{28} representing a hydrogen atom or an alkyl or aralkyl radical, or also R^{28} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{21} representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^{29} radical and an $NR^{30}R^{31}$ radical, R^{29} representing a hydrogen atom or an alkyl or phenyl radical, and R^{30} and R^{31} independently representing alkyl radicals,

R^{22} representing a hydrogen atom or an alkyl radical,

or also R^{21} and R^{22} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{32}R^{33}-$, -O-, -S- and $-NR^{34}-$ radicals, R^{32} and R^{33} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{34} representing a hydrogen atom, an alkyl or aralkyl radical, or also R^{34} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{37} and R^{38} being chosen independently from a hydrogen atom and an alkyl radical or R^{37} and R^{38} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{39}R^{40}-$, -O-, -S- and $-NR^{41}-$ radicals, R^{39} and R^{40} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{41} representing a hydrogen atom or an alkyl radical; and

W represents O or S;

and the pharmaceutically acceptable salts of compounds of general formula **(I)** defined above

as Cdc25 phosphatase inhibitors, and in particular Cdc25-C phosphatase inhibitors, and/or CD45 phosphatase inhibitors. Said compounds can therefore be used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, and/or the CD45 phosphatase.

By alkyl, unless otherwise specified, is meant a linear or branched alkyl radical containing 1 to 12 carbon atoms, preferably 1 to 10 carbon atoms and more preferentially 1 to 8 carbon atoms (and in particular 1 to 6 carbon atoms). By cycloalkyl, unless otherwise specified, is meant a cycloalkyl radical containing 3 to 7 carbon atoms. By carbocyclic or heterocyclic aryl, is meant a carbocyclic or heterocyclic system with 1 to 3 condensed rings comprising at least one aromatic ring, a system being called heterocyclic when at least one of the rings which compose it comprises a heteroatom (O, N or S); when a carbocyclic or heterocyclic aryl radical is called substituted without further specification, it means that said carbocyclic or heterocyclic aryl radical is substituted 1 to 3 times, and preferably 1 to 2 times by radicals different from a hydrogen atom which, unless otherwise specified, are chosen from a halogen atom and the alkyl or alkoxy radicals; moreover, unless otherwise specified, by aryl is meant exclusively a carbocyclic aryl. By haloalkyl, is meant an alkyl radical at least one of the hydrogen atoms of which (and optionally all) is replaced by a halogen atom.

By cycloalkylalkyl, alkoxy, haloalkyl, haloalkoxy and aralkyl radicals, is meant respectively the cycloalkylalkyl, alkoxy, haloalkyl, haloalkoxy and aralkyl radicals, the alkyl, cycloalkyl and aryl radicals of which have the meanings indicated previously.

When it is indicated that a radical is optionally substituted 1 to 3 times, it is preferably optionally substituted 1 to 2 times and more preferentially optionally substituted once.

By linear or branched alkyl having 1 to 6 carbon atoms, is meant in particular the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl, pentyl, neopentyl, isopentyl, hexyl, isohexyl radicals. By haloalkyl, is meant in particular the trifluoromethyl radical. By haloalkoxy, is meant in particular the trifluoromethoxy radical. By carbocyclic aryl, is meant in particular the phenyl and naphthyl radicals. By aralkyl, is meant in particular the phenylalkyl radicals, and in particular the benzyl radical. By saturated carbon-containing cyclic system containing 1 to 3 condensed rings chosen independently from rings with 3 to 7 members, is meant in particular the cyclopropyl, cyclobutyl, cyclohexyl and adamantyl radicals. By heterocyclic or

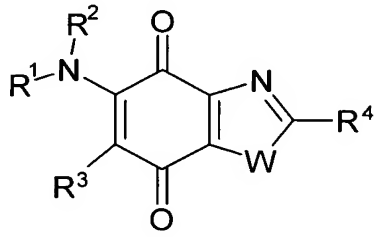
heteroaryl aryl, is meant in particular the thienyl, furanyl, pyrrolyl, imidazolyl, thiazolyl, oxazolyl and pyridyl radicals. Finally, by halogen, is meant fluorine, chlorine, bromine or iodine atoms.

By pharmaceutically acceptable salt, is meant in particular addition salts of inorganic acids such as hydrochloride, hydrobromide, hydroiodide, sulphate, phosphate, diphosphate and nitrate or organic acids such as acetate, maleate, fumarate, tartrate, succinate, citrate, lactate, methanesulphonate, p-toluenesulphonate, pamoate and stearate. Also within the scope of the present invention, when they can be used, are the salts formed from bases such as sodium or potassium hydroxide. For other examples of pharmaceutically acceptable salts, reference can be made to "Salt selection for basic drugs", *Int. J. Pharm.* (1986), **33**, 201-217.

In certain cases, the compounds according to the present invention can comprise asymmetrical carbon atoms. As a result, the compounds according to the present invention have two possible enantiomeric forms, i.e. the "R" and "S" configurations. The present invention includes the two enantiomeric forms and all combinations of these forms, including the "RS" racemic mixtures. In an effort to simplify matters, when no specific configuration is indicated in the structural formulae, it should be understood that the two enantiomeric forms and their mixtures are represented.

Four variants of the compounds of general formula **(I)** can be distinguished:

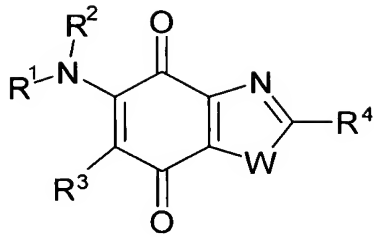
- according to a first variant, the compounds of general formula **(I)** also correspond to general sub-formula $\mathbf{(I)_1}$



$\mathbf{(I)_1}$

in which W represents S and R^1, R^2, R^3 and R^4 have the same meaning as in general formula **(I)**;

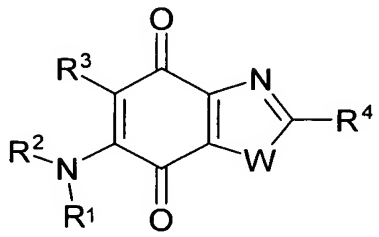
- according to a second variant, the compounds of general formula **(I)** also correspond to general sub-formula $\mathbf{(I)_2}$



(I)$_2$

in which W represents O and R^1, R^2, R^3 and R^4 have the same meaning as in general formula **(I)**;

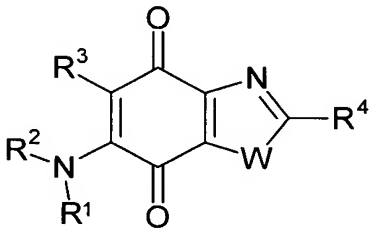
- according to a third variant, the compounds of general formula **(I)** also correspond to general sub-formula **(I)$_3$**



(I)$_3$

in which W represents S and R^1, R^2, R^3 and R^4 have the same meaning as in general formula **(I)**; and

- according to a fourth variant, the compounds of general formula **(I)** also correspond to general sub-formula **(I)$_4$**



(I)$_4$

in which W represents O and R^1, R^2, R^3 and R^4 have the same meaning as in general formula **(I)**.

The compounds of general formula **(I)$_1$** or **(I)$_2$**, or their pharmaceutically acceptable salts can therefore be used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, and/or the CD45 phosphatase. Similarly, the compounds of general formula **(I)$_3$** or **(I)$_4$**, or their pharmaceutically acceptable salts, can be used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, and/or the CD45 phosphatase.

Preferably, the compounds of general formula **(I)**, **(I)$_1$**, **(I)$_2$**, **(I)$_3$** or **(I)$_4$** used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, include at least one of the following characteristics:

- R^1 representing an alkyl, cycloalkyl, alkoxyalkyl, $-(CH_2)-X-Y$, $-(CH_2)-Z-NR^5R^6$ or $-CHR^{35}R^{36}$ radical;
- R^2 representing a hydrogen atom or the methyl, ethyl or benzyl radical;
- R^1 and R^2 forming together with the nitrogen atom a heterocycle with 4 to 8 members (preferably 5 to 7 members, and in particular 6 members) comprising 1 to 2 heteroatoms (and preferably 2 heteroatoms), the members necessary to complete the heterocycle being chosen independently from the $-CH_2-$, -O- and $-NR^{17}$ radicals (and preferably from the $-CH_2-$ and $-NR^{17}-$ radicals), R^{17} representing a methyl or benzyl radical;
- R^3 representing a hydrogen atom, a halogen atom or an alkyl, alkoxy or alkylthio radical;
- R^4 representing an alkyl, $-CH_2-COOR^{18}$ or $-CH_2-CO-NR^{19}R^{20}$ or $-CH_2-NR^{21}R^{22}$ radical or also a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times (and in particular 1 to 3 times) by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy or $NR^{37}R^{38}$ radical.

Generally, for use for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, the compounds of general formula **(I)** in which W represents a sulphur atom are preferred. Another useful alternative for use for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, will nevertheless be the use of the compounds of general formula **(I)** in which W represents an oxygen atom.

Moreover, the X radical will preferably represent a bond or a linear alkylene radical containing 1 to 5 carbon atoms. Preferably also, the Y radical will represent a saturated carbon-containing cyclic system containing 1 to 3 condensed rings chosen independently from rings with 3 to 7 members, or Y will represent a carbocyclic aryl radical optionally substituted (preferably optionally substituted by 1 to 3 radicals chosen from a halogen atom and an alkyl, haloalkyl, alkoxy, haloalkoxy, SO_2NHR^9 or $NR^{10}R^{11}$ radical, and more preferentially optionally substituted by 1 to 3 radicals chosen from a halogen atom and an alkyl, alkoxy, SO_2NHR^9 or $NR^{10}R^{11}$ radical) or also Y will represent an optionally substituted heterocyclic aryl radical, said heterocyclic aryl radical being preferably chosen from the aryl radicals with 5 members (and in particular from the imidazolyl, thienyl or pyridinyl radicals) and preferably optionally substituted by 1 to 3 radicals chosen from a halogen atom and an alkyl, haloalkyl, alkoxy, haloalkoxy, SO_2NHR^9 or $NR^{10}R^{11}$ radical, and more preferentially optionally substituted by 1 to 3 radicals chosen from a halogen atom and an alkyl, alkoxy, SO_2NHR^9 or $NR^{10}R^{11}$ radical; R^9 will preferably represent a hydrogen atom and R^{10} and R^{11} will preferably represent radicals chosen independently from the alkyl radicals. The Z radical will preferably represent an alkylene radical containing 1 to 5 carbon atoms, and in particular a $-(CH_2)_p-$ radical in which p represents an integer from 1 to 3 (p being preferably equal to 1 or 2 and more preferentially equal to 1). Preferably also, R^5 and R^6 are chosen independently from a hydrogen atom and an alkyl radical, or also R^5 and R^6 will form together with the nitrogen atom which carries them a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, said heterocycle then being preferably one of the azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, morpholinyl and thiomorpholinyl radicals optionally substituted by 1 to 3 alkyl radicals (and preferably by 1 to 3 methyl radicals); still more preferentially, R^5 and R^6 are chosen independently from alkyl or alkoxycarbonyl radicals (and in particular R^5 and R^6 are each a methyl radical or *tert*-butoxycarbonyl) or R^5 and R^6 will form together with the nitrogen atom which carries them a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, said heterocycle being then preferably one of the azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, morpholinyl and thiomorpholinyl radicals optionally substituted by 1 to 3 alkyl radicals (and preferably by 1 to 3 methyl radicals). R^{18} will preferably represent a hydrogen atom or the methyl or ethyl radical.

Moreover, the R^7, R^{12}, R^{13}, R^{15}, R^{16}, R^{26}, R^{27}, R^{39} and R^{40} radicals are preferably chosen independently from a hydrogen atom and a methyl radical and the R^8, R^{14}, R^{17}, R^{28} and R^{41} radicals are preferably chosen independently from a hydrogen atom and a methyl or benzyl radical.

Moreover, with respect to R^{19} and R^{20}, the cases will be preferred in which R^{19} represents a hydrogen atom, an alkyl radical or a benzyl radical and R^{20} represents a hydrogen atom or the methyl radical, as well as those in which R^{19} and R^{20} form together with the nitrogen atom which carries them a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, said heterocycle then being preferably one of the azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, morpholinyl and thiomorpholinyl radicals optionally substituted by 1 to 3 alkyl radicals (and preferably optionally substituted by 1 to 3 methyl radicals).

Moreover, with respect to R^{21} and R^{22}, the cases will be preferred in which R^{21} represents a hydrogen atom, an alkyl radical or a benzyl radical and R^{22} represents a hydrogen atom or the methyl radical, as well as those in which R^{21} and R^{22} form together with the nitrogen atom which carries them a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, said heterocycle then being preferably one of the optionally substituted azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, homopiperazinyl, morpholinyl and thiomorpholinyl radicals. With respect to the corresponding R^{32}, R^{33} and R^{34} radicals, these are preferably such that R^{32} and R^{33} are chosen independently from a hydrogen atom and an alkyl radical and preferably from a hydrogen atom and a methyl radical (R^{32} and R^{33} both representing still more preferentially hydrogen atoms) and that R^{34} represents a hydrogen atom, an alkyl radical or a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical (R^{34} representing still more preferentially a hydrogen atom or a methyl or phenyl radical).

Moreover, with respect to R^{35} and R^{36}, the cases will be preferred in which R^{35} and R^{36} form together with the carbon atom which carries them an indanyl radical or R^{35} and R^{36} form together with the carbon atom which carries them a saturated heterocycle containing 5 to 7 members and 1 to 2 heteroatoms chosen from O, N and S, the nitrogen atoms of said heterocycle being optionally substituted by radicals chosen from the alkyl radicals and the benzyl radical.

Moreover, with respect to R^{37} and R^{38}, the cases will be preferred in which R^{37} and R^{38} represent independently radicals chosen from the alkyl radicals.

Finally, when R^4 is a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times, it is preferable that it is chosen from the group consisting of carbocyclic and heterocyclic aryl radicals optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy, haloalkoxy or

$NR^{37}R^{38}$ radical (and in particular 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy or haloalkoxy radical) and the 2,3,4,5-tetrafluorophenyl radical. More preferentially, when R^4 is a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times, R^4 is chosen from the group consisting of carbocyclic and heterocyclic aryl radicals optionally substituted 1 to 2 times by substituents chosen independently from a halogen atom, an alkyl, haloalkyl, alkoxy, haloalkoxy or $NR^{37}R^{38}$ radical (and in particular 1 to 2 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy or haloalkoxy radical), a 3,4,5-trihalophenyl radical and the 2,3,4,5-tetrafluorophenyl radical.

More preferentially, the compounds of general formula **(I)**, $(I)_1$, $(I)_2$, $(I)_3$ or $(I)_4$ used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, include at least one of the following characteristics:

- R^1 representing an alkyl, cycloalkyl, or $-(CH_2)-Z-NR^5R^6$ radical;
- R^2 representing a hydrogen atom or the methyl radical;
- R^3 representing a hydrogen atom, a halogen atom or the methoxy radical;
- R^4 representing an alkyl, $-CH_2-NR^{21}R^{22}$ radical, or also a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times (and in particular 1 to 3 times) by substituents chosen independently from a halogen atom and an alkyl, or $NR^{37}R^{38}$ radical.

Also more preferentially, the compounds of general formula **(I)**, **(I)'**, **(I)"**, $(I)_1$, $(I)_2$, $(I)_3$ or $(I)_4$ used according to the invention include at least one of the following characteristics:

- R^1 representing a $-(CH_2)-Z-NR^5R^6$ radical;
- R^2 representing a hydrogen atom;
- R^3 representing a hydrogen atom or a halogen atom (said halogen atom being preferably a chlorine or bromine atom);
- R^4 representing an alkyl radical or also a phenyl, pyridyl, thienyl or furanyl radical optionally substituted by 1 to 4 (preferably 1 to 3) halogen atoms or by an $NR^{37}R^{38}$ radical.

In still more particularly preferred fashion, the compounds of general formula **(I)**, $(I)_1$, $(I)_2$, $(I)_3$ or $(I)_4$ used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, include at least one of the following characteristics:

- R^3 representing a hydrogen atom or a chlorine atom (and more preferentially a hydrogen atom);
- R^4 representing an alkyl radical or also a phenyl, pyridyl, thienyl or furanyl radical optionally substituted by 1 to 4 (preferably 1 to 3) halogen atoms (and in particular R^4 representing an alkyl radical, and preferably an alkyl radical containing 1 to 4 carbon atoms, and more preferentially also a methyl or ethyl radical).

According to a particular variant of the invention, W represents O. In this particular case, it is preferable that R^1 represents an aryl radical, and in particular a phenyl radical, optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl or alkoxy radical. More preferentially, whenever W represents O, it is preferable that R^1 represents a phenyl radical optionally substituted by a halogen atom (said halogen atom being preferably a fluorine atom).

According to a particular aspect of the invention, R^4 will represent a phenyl radical or a heterocyclic aryl radical with 5 to 6 members optionally substituted 1 to 4 times (and preferably 1 to 3 times) by substituents chosen from the group consisting of halogen atoms, the trifluoromethyl radical and the trifluoromethoxy radical (and preferably chosen from the group consisting of halogen atoms and the trifluoromethyl radical). In particular, said heterocyclic aryl with optionally substituted 5 to 6 members is an optionally substituted pyridine, thiophene, furan or pyrrole ring.

According to another particular aspect, compounds of general formula **(I)** in which W represents S, R^3 represents a hydrogen atom, the substituent $-NR^1R^2$ (the preferences indicated previously for R^1 and R^2 remaining applicable) is attached at position 5 of the benzothiazoledione ring and R^4 is chosen from the alkyl, cycloalkylalkyl, $-CH_2-COOR^{18}$, $-CH_2-CO-NR^{19}R^{20}$ and $-CH_2-NR^{21}R^{22}$ radicals (R^4 being preferably alkyl or cycloalkylalkyl and more preferentially alkyl according to this particular aspect of the invention) are used for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase.

Preferably, the compounds of general formula **(I)**, $(I)_1$, $(I)_2$, $(I)_3$ or $(I)_4$ or their pharmaceutically acceptable salts are used for preparing a medicament intended to treat

a disease chosen from the following diseases / the following disorders: tumorous proliferative diseases, and in particular cancer, non-tumorous proliferative diseases, neurodegenerative diseases, parasitic diseases, viral infections, spontaneous alopecia, alopecia induced by exogenous products, radiation-induced alopecia, auto-immune diseases, transplant rejections, inflammatory diseases and allergies.

Quite particularly, the compounds of general formula **(I)**, **$(I)_1$**, **$(I)_2$**, **$(I)_3$** or **$(I)_4$** or their pharmaceutically acceptable salts can be used for preparing a medicament intended to treat cancer, and in particular breast cancer, lymphomas, cancers of the neck and head, lung cancer, cancer of the colon, prostate cancer and cancer of the pancreas.

According to a particular variant, the compounds of general formula **(I)**, **$(I)_1$**, **$(I)_2$**, **$(I)_3$** or **$(I)_4$** or their pharmaceutically acceptable salts can be used for preparing a medicament intended to treat spontaneous alopecia, alopecia induced by exogenous products or radiation-induced alopecia.

The compounds of general formula **(I)**, **$(I)_1$**, **$(I)_2$**, **$(I)_3$** or **$(I)_4$** can also be used in a method of treatment for tumorous proliferative diseases, and in particular cancer, non-tumorous proliferative diseases, neurodegenerative diseases, parasitic diseases, viral infections, spontaneous alopecia, alopecia induced by exogenous products, radiation-induced alopecia, auto-immune diseases, transplant rejections, inflammatory diseases and allergies, said method comprising the administration of a therapeutically effective dose of a compound of general formula **(I)**, **$(I)_1$**, **$(I)_2$**, **$(I)_3$** or **$(I)_4$** to the patient requiring this treatment.

The pharmaceutical compositions containing a compound of general formula **(I)**, **$(I)_1$**, **$(I)_2$**, **$(I)_3$** or **$(I)_4$**, can be presented in the form of solids, for example powders, granules, tablets, gelatin capsules, liposomes or suppositories. Appropriate solid supports can be, for example, calcium phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidine and wax.

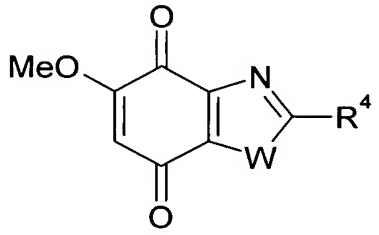
The pharmaceutical compositions containing a compound of general formula **(I)**, **$(I)_1$**, **$(I)_2$**, **$(I)_3$** or **$(I)_4$**, can also be presented in liquid form, for example, solutions, emulsions, suspensions or syrups. Appropriate liquid supports can be, for example, water, organic solvents such as glycerol or the glycols, as well as their mixtures, in varying proportions, in water.

The administration of a medicament according to the invention can be carried out by topical, oral, parenteral route, by intramuscular injection, etc.

The administration dose envisaged for a compound of general formula **(I)**, $(I)_1$, $(I)_2$, $(I)_3$ or $(I)_4$, is comprised between 0.1 mg to 10 g depending on the type of active compound used.

Advantageously, the compounds of general formula **(I)**, $(I)_1$, $(I)_2$, $(I)_3$ or $(I)_4$ can be prepared according to a selective preparation process. Said process makes it possible to substitute either position 5 or position 6 of the benzothiazole-4,7-dione or benzooxazole-4,7-dione nucleus and therefore to obtain a compound of general formula $(I)_1$ and not the corresponding compound of general formula $(I)_3$ (or *vice versa*), or also a compound of general formula $(I)_2$ and not the corresponding compound of general formula $(I)_4$ (or *vice versa*).

The invention therefore relates firstly to a process for the preparation of a compound of general formula $(I)_1$ or $(I)_2$ as defined previously in which R^3 represents a hydrogen atom, said process being characterized in that the compound of general formula **(A)**

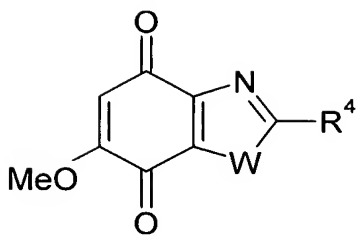


(A)

in which W represents a sulphur atom or an oxygen atom and R^4 has the same meaning as in general formula $(I)_1$ or $(I)_2$ is reacted with an amine of general formula R^1R^2NH in a protic solvent at a temperature preferably comprised between 20°C and the boiling temperature of the solvent.

Preferably, the protic solvent for the abovementioned process is chosen from ethanol and methanol.

The invention relates in particular to a process for the preparation of a compound of general formula $(I)_3$ or $(I)_4$ as defined previously in which R^3 represents a hydrogen atom, said process being characterized in that the compound of general formula **(K)**



(K)

in which W represents a sulphur atom or an oxygen atom and R^4 has the same meaning as in general formula $(I)_3$ or $(I)_4$ is reacted with an amine of general formula R^1R^2NH in a protic solvent at a temperature preferably comprised between 20°C and the boiling temperature of the solvent.

Preferably, the protic solvent for the abovementioned process is chosen from ethanol and methanol.

The invention also relates, as novel products, to the compounds of general formula **(A)** in which W and R^4 have the meaning indicated previously, it being understood however that if W represents a sulphur atom then R^4 is not methyl, as well as the salts of the latter.

The invention thus relates in particular, as novel products, to the compounds of general formula **(A)** in which W represents an oxygen atom (hereafter respectively the compounds of general formula **(A')**), as well as the salts of the latter.

It similarly relates to the compounds of general formula **(A)** in which W represents a sulphur atom and R^4 has the meaning indicated previously but does not represent methyl (hereafter respectively the compounds of general formula **(A'')**), as well as the salts of the latter. Preferably, the compounds of general formula **(A'')** or their salts are such that R^4 has the meaning indicated previously but does not represent alkyl.

The invention also relates, as novel products, to the compounds of general formula **(K)** in which W and R^4 have the meaning indicated previously, it being understood however that if W represents a sulphur atom then R^4 is not the phenyl group (but can be a substituted phenyl group), as well as the salts of the latter.

The invention therefore in particular relates, as novel products, to the compounds of general formula **(K)** in which W represents an oxygen atom (hereafter respectively the compounds of general formulae **(K')**), as well as the salts of the latter.

It relates similarly to the compounds of general formula **(K)** in which W represents a sulphur atom and R^4 has the meaning indicated previously but does not represent the phenyl group (but can be a substituted phenyl group), compounds hereafter called the compounds of general formula **(K'')**, as well as the salts of the latter. Preferably, the compounds of general formula **(K'')** or their salts are such that R^4 represents a phenyl group substituted by at least one halogen atom or also such that R^4 represents an alkyl radical.

The invention also relates to the compounds of general formula **(I)** chosen from the following compounds:

- 2-(2-chloro-6-fluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione;

- 2-(2-chloro-6-fluorophenyl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione;

as well as the salts of the latter;

The invention also relates, as medicaments, to said compounds or their pharmaceutically acceptable salts. It relates moreover to the pharmaceutical compositions comprising, as active ingredient, one of said compounds or a pharmaceutically acceptable salt of the latter, as well as at least one pharmaceutically acceptable excipient.

A subject of the invention is also the use of said compounds or their pharmaceutically acceptable salts for preparing a medicament intended to inhibit the Cdc25 phosphatases, and in particular the Cdc25-C phosphatase, and/or the CD45 phosphatase. Preferably, said compounds or their pharmaceutically acceptable salts are used for preparing a medicament intended to treat a disease chosen from the following diseases / the following disorders: tumorous proliferative diseases, and in particular cancer, non-tumorous proliferative diseases, neurodegenerative diseases, parasitic diseases, viral infections, spontaneous alopecia, alopecia induced by exogenous products, radiation-induced alopecia, auto-immune diseases, transplant rejections, inflammatory diseases and allergies. Quite particularly, said compounds or their pharmaceutically acceptable salts can be used for preparing a medicament intended to treat cancer, and in particular breast cancer, lymphomas, cancers of the neck and head, lung cancer, cancer of the colon, prostate cancer and cancer of the pancreas.

The compounds of general formula **(I)** can be prepared by the processes described hereafter.

Preparation of the compounds of general formula (I)

The preparation processes hereafter are given by way of illustration and a person skilled in the art can subject them to the variations that he deems useful, both with respect to the reagents and to the reaction conditions and techniques.

According to the present invention, the processes hereafter can be used in order to obtain exclusively a compound of general formula $(I)_1$ and not the corresponding compound of general formula $(I)_3$ (or *vice versa*), or also a compound of general formula $(I)_2$ and not the corresponding compound of general formula $(I)_4$ (or *vice versa*).

A) ***Process for the preparation of the regioisomers of general formula $(I)_1$ or $(I)_2$***

Generally, the compounds of general formula $(I)_1$ or $(I)_2$ in which R^3 represents H can be prepared according to the method illustrated in Diagram 1 hereafter.

(A)

$(I)_1$: W = S
$(I)_2$: W = O

Diagram 1

According to this method, the compounds of general formula $(I)_1$ or $(I)_2$, in which W, R^1, R^2 and R^4 are as defined above and R^3 represents H, are obtained by treatment of the compounds of general formula **(A)** with amines of general formula R^1R^2NH in a protic solvent such as methanol or ethanol, at a temperature preferably comprised between 25°C and the boiling temperature of the solvent (Yasuyuki Kita et al., *J. Org. Chem.* (1996), **61**, 223-227).

In the case where it is also desired to substitute position 6 of the benzothiazoledione or benzoxazoledione nucleus (compounds of general formula $(I)_1$ or $(I)_2$ in which $R^3 \neq H$), it is sufficient to carry out an additional substitution using the conditions familiar to a person skilled in the art.

i) W represents a sulphur atom:

Preparation of the intermediates of general formula (A)

When W represents a sulphur atom, the intermediates of general formula **(A)** can be prepared according to the process represented in Diagram 2 hereafter.

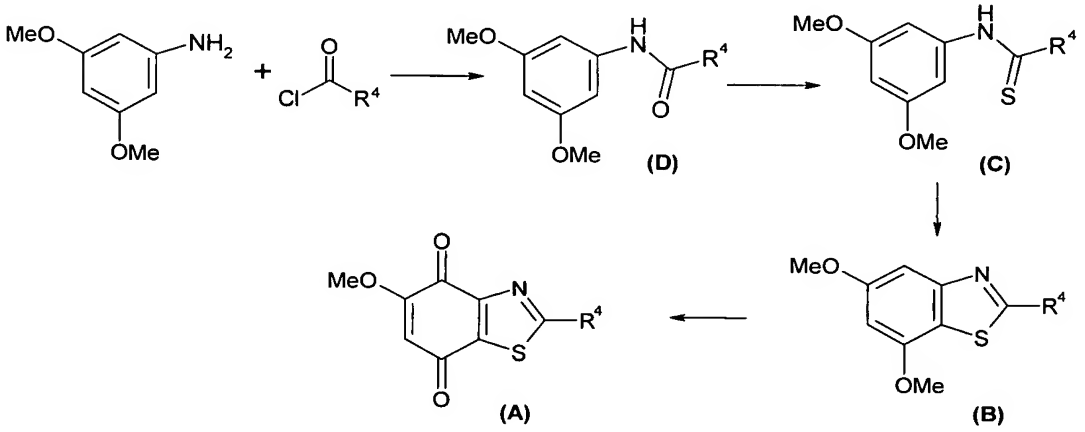


Diagram 2

The compounds of general formula **(A)** in which R^4 is as defined above can be obtained by oxidative demethylation of the compounds of general formula **(B)**, for example by treatment with chromium oxide (VI) in acetic acid (J. M. de L. Vanderlei et al., *Tetrahedron: Asymmetry* (1997), 8 (**16**), 2781-2785), or by treatment with a 50% hydrogen peroxide solution in the presence of phosphomolybdic acid and formic acid (A. S. Chida et al., *Synth Commun* (2001), **5**, 657-660), or also by treatment with dichlorodicyanoquinone (DDQ) in an H_2O/THF mixture (K. Narayanan, *Heterocycles* (1991), **10**, 2005-2014) or also by treatment with cerium ammonium nitrate in an equimolar acetonitrile / water or ethyl acetate / water mixture under vigorous stirring at ambient temperature.

The nitrated compound of general formula **(B.i)** can be obtained by treatment of the compound of general formula **(B)** with cerium ammonium nitrate (CAN). The compound of general formula **(A)** can then be obtained after reduction of the nitro group by the action of hydrogen in the presence of palladium on carbon or by the action

of tin chloride in order to obtain the intermediate of general formula **(B.ii)** which is then oxidized in order to finally produce the quinone of general formula **(A)** by the action of cerium ammonium nitrate (cf. Diagram 3 hereafter; K. Mohri et al., *Chem Pharm Bull*, (1998), **12**, 1872-1877).

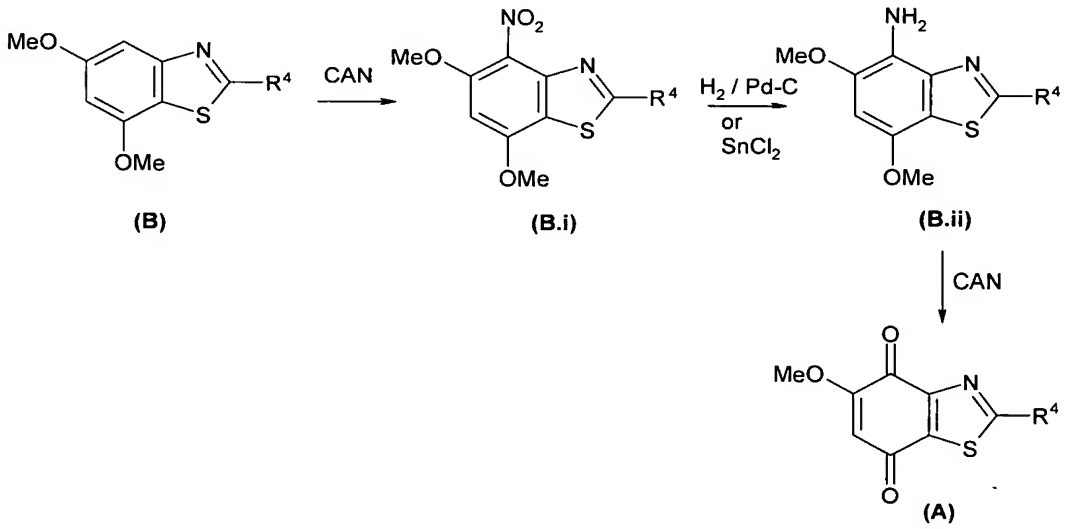


Diagram 3

*Preparation of the intermediates of general formula **(B)***

The compounds of general formula **(B)**, in which R^4 is as defined above, can be obtained in 3 stages (M. A. Lyon et al., *J. Chem. Soc., Perkin Trans 1*, (1999), 437-442) from 3,5-dimethoxyaniline converted successively to amide **(D)** by the action of the corresponding acid chloride according to standard methods known to a person skilled in the art. The amides of general formula **(D)** are then converted to thioamides of general formula **(C)** by treatment with Lawesson's reagent in dry toluene at a temperature preferably comprised between 80°C and reflux for a duration preferably comprised between 2 hours and 18 hours, or by potassium pentasulphide in DME at a temperature preferably comprised between 85°C and reflux. The thioamides of general formula **(C)** are then treated with potassium ferricyanide in aqueous medium in the presence of soda according to the method of Jacobson (P. Jacobson, *Chem. Ber.* (1886), **19**, 1067) in order to produce the compounds of general formula **(B)**.

ii) W represents an oxygen atom:

*Preparation of the intermediates of general formula **(A)***

When W represents an oxygen atom, the intermediates of general formula **(A)** can be prepared according to the process represented in Diagram 4 below.

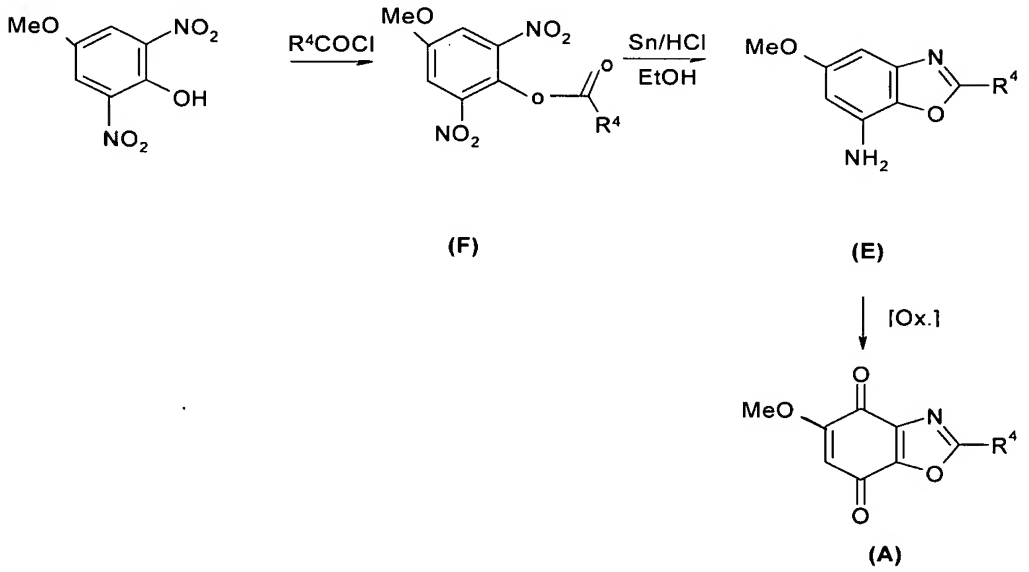


Diagram 4

The compounds of general formula **(A),** in which R^4 is as defined above, can be obtained in 3 stages from 4-methoxy-2,6-dinitrophenol (described in particular by P. Cotelle and J.-P. Catteau, *Synth. Commun.*, **26**, (1996), 4105-4112), which, once esterified in order to produce the intermediate of general formula **(F)** according to the usual methods known to a person skilled in the art can be subjected to the action of a reducing agent under dehydrating conditions (such as, for example, tin and hydrogen chloride in ethanol described by Y.A.M. Marghlani et al. *Pakistan J. Sci. Ind. Res.*, **23**, (1980), 166-168) in order to provide a 7-amino-5-methoxy-benzoxazole derivative of general formula **(E)**. The 7-amino function of the compound of general formula **(E)** then allows its oxidation to be achieved in order to produce the compound of general formula **(A)** according to processes described previously.

It is also possible to envisage the preparation of intermediates of general formula **(A)** in which W represents an oxygen atom according to the process described in Diagram 4*a* hereafter.

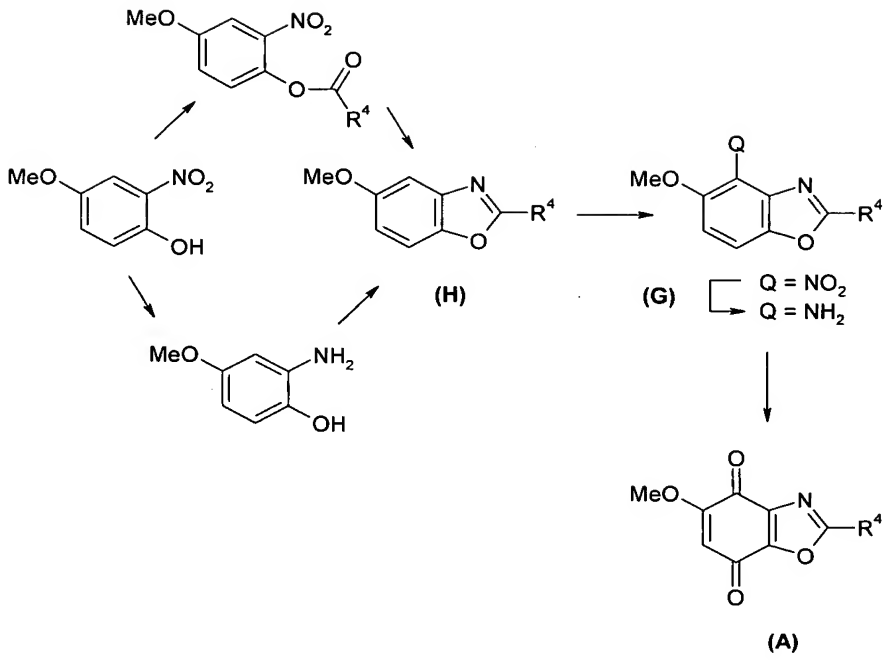


Diagram 4*a*

According to the alternative synthesis presented in Diagram 4*a*, 4-methoxy-2-nitrophenol (commercial) is converted to 5-methoxy-benzoxazole derivative of general formula **(H),** either by dehydrating esterification/reduction of Diagram 4, or by reduction followed by condensation described previously. The intermediate of general formula **(H)** is then nitrated and reduced to the corresponding amine according to a method already described above (cf. Diagram 3), then oxidized as previously to the quinone of general formula **(A)**.

B) ***Process for the preparation of the regioisomers of general formula (I)$_3$ or (I)$_4$***

Generally, the compounds of general formula **(I)$_3$** or **(I)$_4$** in which R^3 represents H can be prepared according to the method illustrated in Diagram 5 hereafter.

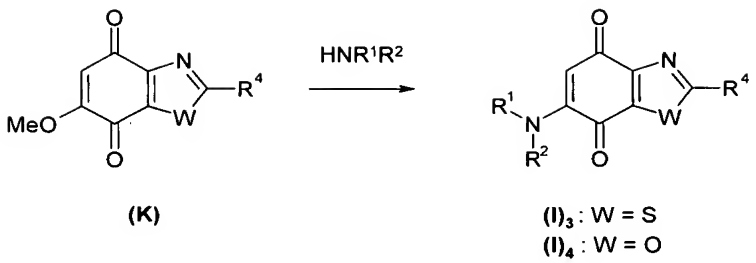


Diagram 5

According to this method, the compounds of general formula $(I)_3$ or $(I)_4$, in which W, R^1, R^2 and R^4 are as defined above and R^3 represents H, are obtained by treatment of the compounds of general formula **(K)** with amines of general formula R^1R^2NH in a protic solvent such as methanol or ethanol, at a temperature preferably comprised between 25°C and the boiling temperature of the solvent (Yasuyuki Kita et al., *J. Org. Chem.* (1996), **61**, 223-227).

In the case where it is also desired to substitute position 6 of the benzothiazoledione or benzoxazoledione nucleus (compounds of general formula $(I)_3$ or $(I)_4$ in which $R^3 \neq H$), it is sufficient to carry out an additional substitution using conditions familiar to a person skilled in the art.

i) W represents a sulphur atom:

Preparation of the intermediates of general formula (K)

When W represents a sulphur atom, the intermediates of general formula **(K)** can be prepared according to the process represented in Diagram 6 hereafter.

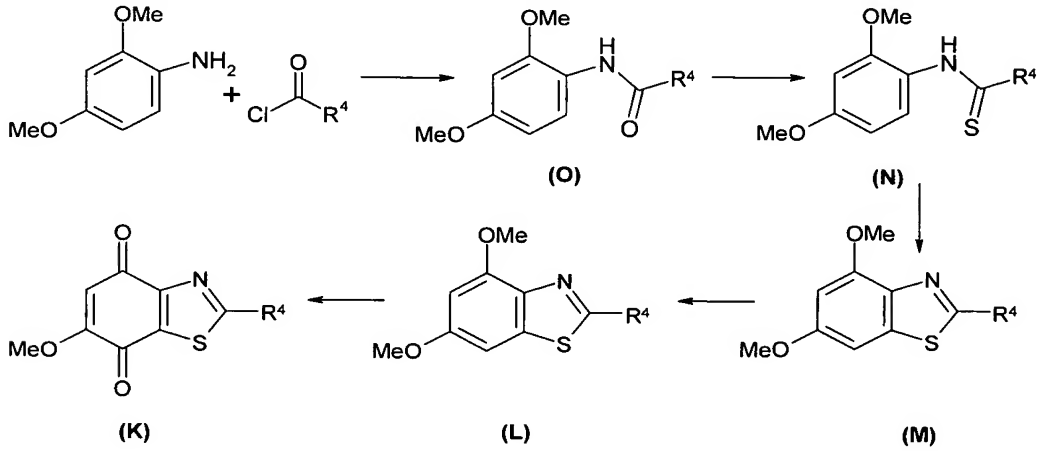


Diagram 6

The compounds of general formula **(K)** in which R^4 is as defined above can be obtained according to a process analogous to that described for the preparation of the intermediates of general formula **(A)** (cf. Diagrams 2 and 3), the starting product being 2,4-dimethoxyaniline (commercial).

ii) W represents an oxygen atom:

Preparation of the intermediates of general formula (K)

When W represents an oxygen atom, the intermediates of general formula **(K)** can be prepared according to the process represented in Diagram 7 hereafter.

Diagram 7

The methods presented in Diagram 7 are analogous to those presented in Diagram 4, but this time the starting product is 5-methoxy-2-nitro-resorcinol (described in particular by J.F. Grove et al. *J. Chem. Soc.* (1956), 1956-1963).

Alternatively, the method represented in Diagram 8 hereafter can also be used.

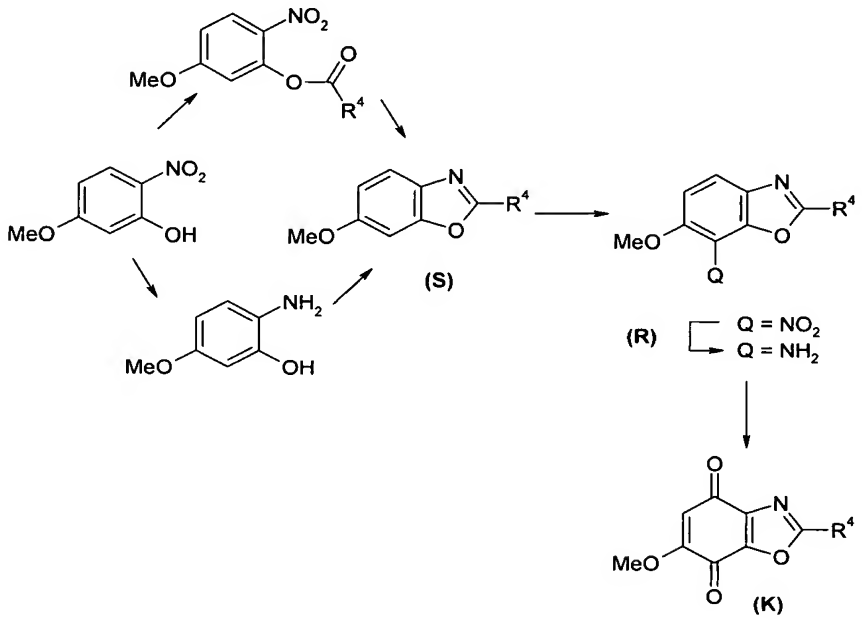


Diagram 8

According to this method, (commercial) 5-methoxy-2-nitrophenol is converted to 6-methoxy-benzoxazole derivative of general formula **(S)**, either using a dehydrating esterification/reduction reaction as presented in Diagram 4, or by reduction followed by condensation described previously. The intermediate of general formula **(S)** is then nitrated and reduced to the corresponding amine of general formula **(R)** according to the process presented in Diagram 3, then oxidized as previously to the quinone of general formula **(K)**.

As regards the temperatures referred to in the present text, the term "approximately *XX*°C" indicates that the temperature in question corresponds to a range of more or less 10°C, either side of the temperature *XX*°C, and preferably to a range of more or less 5°C, either side of the temperature *XX*°C.

Unless otherwise specified, all the technical and scientific terms used here have the same meaning as that usually understood by an ordinary specialist in the field to which this invention belongs. Similarly, all the publications, patent applications, all the patents and all other references mentioned here are incorporated by way of reference.

The following examples are presented in order to illustrate the above procedures and should in no event be considered as a limit to the scope of the invention.

EXAMPLES

Method used for measuring the retention time (r.t.) and the molecular peak (MH+)

The compounds are characterized by their retention time (r.t.), expressed in minutes, determined by liquid chromatography (LC), and their molecular peak (MH+) determined by mass spectrometry (MS), a single quadripole mass spectrometer (Micromass, Platform model) equipped with an electrospray source is used with a resolution of 0.8 Da at 50% valley.

For the examples below, the elution conditions corresponding to the results indicated are the following: transition of an acetonitrile-water-trifluoroacetic acid mixture 50-950-0.2 (A) to an acetonitrile-water mixture 950-50 (B) via a linear gradient over a period of 8.5 minutes, then elution with the pure mixture B for 10.5 minutes.

Example 1: 2-(2,6-difluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione:

1.1) *N-(3,5-dimethoxyphenyl)-2,6-difluorobenzamide:*

5.5 ml (39.2 mmol; 1.2 equivalent) of triethylamine and 4.5 ml (35.9 mmol; 1.1 equivalent) of 2,6-difluorobenzoyl chloride are added to 5 g (32.6 mmol) of 3,5-dimethoxyaniline in solution in 100 ml of anhydrous toluene. The reaction medium is maintained under stirring at 70°C for 1 hour 30 minutes, then, after returning to ambient temperature, washed with 3 times 50 ml of water. The resulting organic phase is dried over magnesium sulphate then the solvent is evaporated off under reduced pressure. The expected product is obtained in the form of a white powder (8.75 g; yield = 97 %) used in the following stage without other purification.
MS-LC: MH+ = 294.11; r.t. = 9.93 min.

1.2) *N-(3,5-dimethoxyphenyl)-2,6-difluorobenzenecarbothioamide*:

20.3 g (50 mmol; 1.5 equivalents) of Lawesson's reagent is added to 9.8 g (33.4 mmol) of *N*-(3,5-dimethoxyphenyl)-2,6-difluorobenzamide in solution in 150 ml of anhydrous toluene. The reaction medium is maintained under stirring at 120°C for 8 hours, then, after returning to ambient temperature, is washed with 3 times 75 ml of water. The resulting organic phase is dried over magnesium sulphate then the solvent is evaporated off under reduced pressure. The residue is purified by chromatography on a silica column (eluent: dichloromethane/methanol 98/2) and the expected product is obtained in the form of a green oil (10 g; yield = 96 %).
MS-LC: MH+ = 310.06; r.t. = 10.53 min.

1.3) *2-(2,6-difluorophenyl)-5,7-dimethoxy-1,3-benzothiazole:*

170 ml (103 mmol; 3 equivalents) of a freshly prepared 20% aqueous solution of potassium ferricyanide is added to 10.3 g (33.3 mmol) of *N*-(3,5-dimethoxyphenyl)-2,6-difluorobenzenecarbothioamide dissolved in 150 ml of a 1.5*M* soda solution. The reaction medium is maintained under stirring at ambient temperature for 24 hours, then the beige precipitate formed is filtered, washed with water and dried (6.8 g; yield = 66%). The mother liquors can be extracted by 3 times 75 ml of dichloromethane, then the organic phases are washed with a saturated solution of sodium chloride. After concentration under reduced pressure, the residue obtained can be purified on a silica

column (eluent: ethyl acetate/heptane: 1/3) in order to provide another 2 g of expected product (overall yield = 86%). Melting point: 136-138°C.
NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.65 (m, 1H, arom. H); 7.36-7.31 (m, 3H, arom. H); 6.75 (m, 1H, arom. H); 3.96 (s, 3H, CH_3); 3.87 (s, 3H, CH_3).
MS-LC: MH+ = 308.12; r.t. = 11.48 min.

1.4) *2-(2,6-difluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione:*

1.4.1) *2-(2,6-difluorophenyl)-5,7-dimethoxy-4-nitro-1,3-benzothiazole:*

A solution of 16 g (29.3 mmol; 3 equivalents) of cerium ammonium nitrate in 40 ml of water is added dropwise to 3 g (9.76 mmol) of 2-(2,6-difluorophenyl)-5,7-dimethoxy-1,3-benzothiazole in solution in 75 ml of ethyl acetate. The reaction mixture is maintained under stirring for 2 hours at ambient temperature, then washed with 3 times 20 ml of water. The organic phases are dried over magnesium sulphate, filtered then concentrated under reduced pressure. The residue is purified by chromatography on a silica column (eluent: ethyl acetate/heptane: 3/7). Two fractions are separated:

0.3 g (yield = 10%) of 2-(2,6-difluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione is obtained in the form of yellow powder.
MS-LC: MH+ = 308.08; r.t. = 10 min.

1.5 g of 2-(2,6-difluorophenyl)-5,7-dimethoxy-4-nitro-1,3-benzothiazole (45% yield) is obtained in the form of orange-coloured powder.
NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.72 (m, 1H, arom. H); 7.38 (m, 2H, arom. H); 7.11 (m, 1H, arom. H); 4.12 (s, 3H, CH_3); 4.07 (s, 3H, CH_3).
MS-LC: MH+ = 353.05; r.t. = 11.30 min.

1.4.2) *2-(2,6-difluorophenyl)-5,7-dimethoxy-1,3-benzothiazol-4-amine:*

230 mg (0.65 mmol) of intermediate 1.4.1 dissolved in 15 ml of concentrated hydrochloric acid is reacted with 0.5 g (2.2 mmol; 3.4 equivalents) of dihydrated tin chloride in 5 ml of water. The reaction mixture is maintained under stirring for 2 hours at 50°C, then after returning to ambient temperature, poured on ice before being neutralized with a 5*M* soda solution. The product is then extracted with 3 times 15 ml of dichloromethane, the organic phases are combined, washed with a saturated solution of sodium chloride, dried over magnesium sulphate, filtered, then, after concentration under reduced pressure, the expected product is obtained in the form of a yellow oil. It is used in the following stage without other purification.

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.67 (m, 1H, arom. H); 7.34 (m, 2H, arom. H); 6.92 (s, 1H, arom. H); 3.91 (s, 3H, CH_3); 3.90 (s, 3H, CH_3).
MS-LC: MH+ = 323.10; r.t. = 9.86 min.

1.4.3) *2-(2,6-difluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione:*

A solution of 1.22 g of cerium ammonium nitrate (2.23 mmol, 2.1 equivalents) in 8 ml of water is added to 343 mg (1.06 mmol) of 2-(2,6-difluorophenyl)-5,7-dimethoxy-1,3-benzothiazol-4-amine in solution in 25 ml of ethyl acetate. The reaction mixture is maintained under vigorous stirring at ambient temperature for 1 hour 30 minutes then the organic phase is separated and washed with 3 times 20 ml of water, then dried over magnesium sulphate, filtered and the solvent is evaporated off under reduced pressure. The residue is purified by chromatography on a silica column (eluent: ethyl acetate/heptane: 3/7) and 280 mg (yield = 86%) of 2-(2,6-difluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione is obtained in the form of yellow powder.
NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.72 (m, 1H, arom. H); 7.39 (m, 2H, arom. H); 6.32 (s, 1H, CH); 3.88 (s, 3H, CH_3).
MS-LC: MH+ = 308.05; r.t. = 9.99 min.

1.5) *2-(2,6-difluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione:*

104 ml (0.95 mmol; 1.5 equivalents) of N,N-dimethylethylenediamine is added to 195 mg of 2-(2,6-difluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione in solution in 20 ml of anhydrous ethanol. The reaction mixture is stirred at 70°C for 2 hours then the solvent is evaporated off under reduced pressure. The residue is purified on a silica column (eluent: 5% methanol in dichloromethane). 130 mg (yield = 57%) of expected compound is obtained in the form of a red powder.
NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.72 (m, 1H, arom. H); 7.52 (m, 1H, NH.); 7.38 (m, 2H, arom. H); 5.60 (s, 1H, CH); 3.28 (m, 2H, CH_2); 2.53 (m, 2H, CH_2); 2.20 (s, 6H, $2CH_3$).
MS-LC: MH+ = 364.14; r.t. = 7.85 min.

The compounds of Examples 2 to 7 are obtained in a similar manner to that described for Example 1, with appropriate acyl chlorides replacing 2,6-difluorobenzoyl chloride in the first stage and N-(2-aminoethyl)pyrrolidine replacing N,N-dimethylethylenediamine in the last stage for Examples 3, 5 and 7.

Example 2: 2-(2,5-dichlorothien-3-yl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione:

2.1) *2,5-dichloro-N-(3,5-dimethoxyphenyl)thiophene-3-carboxamide:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 10.20 (s, 1H, NH); 7.47 (s, 1H, arom. H); 6.95 (s, 1H, arom. H); 6.27 (s, 1H, arom. H); 3.72 (s, 6H, $2CH_3$).
MS-LC: MH+ = 332.01; r.t. = 11.08 min.

2.2) *2,5-dichloro-N-(3,5-dimethoxyphenyl)thiophene-3-carbothioamide:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 11.96 (s, 1H, NH); 7.30 (s, 1H, arom. H); 7.25 (s, 1H, arom. H); 6.44 (s, 1H, arom. H); 3.74 (s, 6H, $2CH_3$).
MS-LC: MH+ = 348.00; r.t. = 11.55 min.

2.3) *2-(2,5-dichlorothien-3-yl)-5,7-dimethoxy-1,3-benzothiazole:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.72 (s, 1H, arom. H); 7.22 (s, 1H, arom. H); 6.73 (s, 1H, arom. H); 3.96 (s, 3H, CH_3); 3.86 (s, 3H, CH_3).
MS-LC: MH+ = 345.94; r.t. = 12.77 min.

2.4) *2-(2,5-dichlorothien-3-yl)-5-methoxy-1,3-benzothiazole-4,7-dione:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.75 (s, 1H, arom. H); 6.31 (s, 1H, CH); 3.88 (s, 3H, CH_3).
MS-LC: MH+ = 345.98; r.t. = 11.52 min.

2.5) *2-(2,5-dichlorothien-3-yl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.72 (s, 1H, arom. H); 7.51 (m, 1H, NH.); 5.58 (s, 1H, CH); 3.36 (m, 2H, CH_2); 2.54 (m, 2H, CH_2); 2.20 (s, 6H, $2CH_3$).
MS-LC: MH+ = 402.06; r.t. = 8.42 min.

Example 3: 2-(2,5-dichlorothien-3-yl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione:

MS-LC: MH+ = 427.97; r.t. = 8.70 min.

Example 4: 5-{[2-(dimethylamino)ethyl]amino}-2-(4-fluorophenyl)-1,3-benzothiazole-4,7-dione:

4.1) *N-(3,5-dimethoxyphenyl)-4-fluorobenzamide:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 10.15 (s, 1H, NH); 8.01 (m, 2H, arom. H); 7.36 (m, 2H, arom. H); 7.05 (m, 2H, arom. H); 6.26 (s, 1H, arom. H); 3.73 (s, 6H, $2CH_3$).
MS-LC: MH+ = 276.17; r.t. = 10.07 min.

4.2) *N-(3,5-dimethoxyphenyl)-4-fluorobenzenecarbothioamide:*

MS-LC: MH+ = 292.17; r.t. = 10.72 min.

4.3) *2-(4-fluorophenyl)-5,7-dimethoxy-1,3-benzothiazole:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 8.11 (m, 2H, arom. H); 7.40 (m, 2H, arom. H); 7.22 (s, 1H, arom. H); 6.69 (s, 1H, arom. H); 3.95 (s, 3H, CH_3); 3.86 (s, 3H, CH_3).
MS-LC: MH+ = 290.07; r.t. = 11.93 min.

4.4) *2-(4-fluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 8.15 (m, 2H, arom. H); 7.42 (m, 2H, arom. H); 6.28 (s, 1H, CH); 3.87 (s, 3H, CH_3).
MS-LC: MH+ = 290.14; r.t. = 11.95 min.

4.5) 5-{[2-(dimethylamino)ethyl]amino}-2-(4-fluorophenyl)-1,3-benzothiazole-4,7-dione:

NMR ^{1}H (DMSO d6, 400 MHz, δ): 8.11 (m, 2H, arom. H); 7.48 (m, 1H, NH); 7.41 (m, 2H, arom. H); 5.57 (s, 1H, CH); 3.26 (m, 2H, CH_2); 2.55 (m, 2H, CH_2); 2.22 (s, 6H, $2CH_3$).
MS-LC: MH+ = 346.18; r.t. = 8.01 min.

Example 5: 2-(4-fluorophenyl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione:

NMR ^{1}H (DMSO d6, 400 MHz, δ): 8.12 (m, 2H, arom. H); 7.58 (m, 1H, NH); 7.41 (m, 2H, arom. H); 5.55 (s, 1H, CH); 3.41 (m, 2H, CH_2); 2.69 (m, 2H, CH_2); 2.51 (m, 2H, CH_2); 2.44 (m, 2H, CH2); 1.70 (m, 4H, 2CH2).
MS-LC: MH+ = 372.19; r.t. = 8.12 min.

Example 6: 2-(2-chloro-6-fluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione:

6.1) *2-chloro-N-(3,5-dimethoxyphenyl)-6-fluorobenzamide:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 10.69 (s, 1H, NH); 7.53 (m, 1H, arom. H); 7.43 (m, 1H, arom. H); 7.37 (m, 1H, arom. H); 6.93 (m, 2H, arom. H); 6.29 (s, 1H, arom. H); 3.72 (s, 6H, $2CH_3$).
MS-LC: MH+ = 310.15; r.t. = 10.11 min.

6.2) *2-chloro-N-(3,5-dimethoxyphenyl)-6-fluorobenzenecarbothioamide:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.41 (m, 2H, arom. H); 7.27 (m, 3H, arom. H); 6.46 (s, 1H, arom. H); 3.75 (s, 6H, $2CH_3$).
MS-LC: MH+ = 326.09; r.t. = 10.73 min.

6.3) *2-(2-chloro-6-fluorophenyl)-5,7-dimethoxy-1,3-benzothiazole:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.66 (m, 1H, arom. H); 7.56 (m, 1H, arom. H); 7.47 (m, 1H, arom. H); 7.30 (s, 1H, arom. H); 6.77 (s, 1H, arom. H); 3.96 (s, 3H, CH_3); 3.88 (s, 3H, CH_3).
MS-LC: MH+ = 324.03; r.t. = 11.60 min.

6.4) *2-(2-chloro-6-fluorophenyl)-5-methoxy-1,3-benzothiazole-4,7-dione:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.69 (m, 1H, arom. H); 7.61 (m, 1H, arom. H); 7.52 (m, 1H, arom. H); 6.32 (s, 1H, CH); 3.88 (s, 3H, CH_3).
MS-LC: MH+ = 324.03; r.t. = 9.23 min.

6.5) *2-(2-chloro-6-fluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione:*

NMR ^{1}H (DMSO d6, 400 MHz, δ): 7.67 (s, 1H, arom. H); 7.59 (m, 1H, arom. H); 7.55 (m, 1H, NH.); 7.49 (m, 1H, arom. H); 5.61 (s, 1H, CH); 3.36 (m, 2H, CH_2); 2.54 (m, 2H, CH_2); 2.19 (s, 6H, $2CH_3$).
MS-LC: MH+ = 380.10; r.t. = 7.88 min.

Example 7: 2-(2-chloro-6-fluorophenyl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione:

MS-LC: MH+ = 406.10; r.t. = 8.01 min.

Pharmacological study of the compounds of the invention

Test protocols

i) Measurement of the phosphatase activity of the purified Cdc25C recombinant enzyme

The phosphatase activity of the MBP-Cdc25C protein is evaluated by dephosphorylation of 3-O-methylfluorescein-phosphate (OMFP) to 3-O-methylfluorescein (OMF) with determination of the fluorescence of the reaction product at 475 nm. This test allows identification of the inhibitors of Cdc25 recombinant enzyme. The preparation of the fusion protein MBP-Cdc25C is described in PCT Patent Application WO 01/44467.

The reaction is carried out in 384-well plate format in a final volume of 50 µl. The MBP-Cdc25C protein (prepared as described above) is stored in the following elution buffer: 20 mM Tris-HCl pH 7.4; 250 mM NaCl; 1mM EDTA; 1 mM of dithiothreitol (DTT); 10 mM maltose. It is diluted to a concentration of 60 µM in the following reaction buffer: 50 mM Tris-HCl pH 8.2; 50 mM NaCl; 1 mM DTT; 20% glycerol. Measurement of the background noise is carried out with the buffer without addition of the enzyme. The products are tested at decreasing concentrations starting from 40 µM. The reaction is initiated by the addition of an OMFP solution at 500 µM final (prepared extemporaneously from a 12.5 mM stock solution in 100% DMSO (Sigma #M2629)). After 4 hours at 30°C in a disposable 384-well plate, the fluorescence measured at OD 475 nm is read using a Victor^2 plate reader (EGG-Wallac). Determination of the 50% inhibitory concentration of the enzymatic reaction is calculated from three independent experiments. Only the values included in the linear part of the sigmoid are retained for linear regression analysis.

ii) Measurement of the tyrosine phosphatase activity of the CD45 enzyme:

Measurement of the tyrosine phosphatase activity of CD45 is based on the dephosphorylation of the peptide pp60$^{c\text{-}src}$ by CD45. Only the cytoplasmic domain of purified human CD45 enzyme (amino acids 584 to 1281, molecular weight = 95 kDa) expressed in a yeast expression system is used for the measurement. The substrate is a synthetic peptide based on the sequence of the negative regulatory domain of pp60$^{c\text{-}src}$. The released phosphate is measured by a malachite green type reagent.

The reaction is carried out in 384-well plate format with a final volume of 20 µl. The substrate pp60$^{c\text{-}src}$ (P-301, BIOMOL, Plymouth Meeting, PA, USA) is diluted to a

concentration of 925 µM in the following reaction buffer: 50 mM Hepes pH 7.2; 1 mM EDTA; 1 mM of dithiothreitol (DTT); 0.05% NP-40 surfactant. The final substrate concentration is 185 µM. The candidate products are tested in a range of decreasing concentrations starting from 160 µM. The reaction is initiated by adding CD45 (SE-135, BIOMOL, Plymouth Meeting, PA, USA) at 15 U/µl (1 U = 1 pmol/min) diluted in reaction buffer. The final enzyme concentration is 1.75 U/µl. After incubation for 1 hour at 30°C, BIOMOL Green Reagent (AK-111, BIOMOL, Plymouth Meeting, PA, USA) is added in a volume of 50 µl / well. After 20 to 30 minutes during which the colour develops, the absorbance at 620 nm is read using a Victor^2 plate reader (EGG-Wallac). Determination of the 50% inhibitory concentration of the enzyme reaction is calculated from three independent experiments.

iii) *Characterization of the antiproliferative activity*:

By way of example, the effect of a treatment on two human cell lines Mia-Paca2 and DU145 by the compounds of the examples described previously will be studied. The cell lines DU145 (human prostate cancer cells) and Mia-PaCa2 (human pancreas cancer cells) were acquired from the American Tissue Culture Collection (Rockville, Maryland, USA). The cells placed in 80 µl of Dulbecco's Modified Eagle's medium (Gibco-Brl, Cergy-Pontoise, France) completed with 10% foetal calf serum inactivated by heating (Gibco-Brl, Cergy-Pontoise, France), 50,000 units/l of penicillin and 50 mg/l of streptomycin (Gibco-Brl, 10378-057, Cergy-Pontoise, France), and 2 mM of glutamine (Gibco-Brl, Cergy-Pontoise, France) were seeded on a 96-well plate on day 0. The cells were treated on day 1 for 96 hours with increasing concentrations of each of the compounds to be tested up to 10 µM. At the end of this period, quantification of cell proliferation is evaluated by a colorimetric test based on the cleavage of the tetrazolium salt WST1 by the mitochondrial dehydrogenases in viable cells leading to the formation of formazan (Boehringer Mannheim, Meylan, France). These tests are carried out in duplicate with 8 determinations per concentration tested. For each compound to be tested, the values included in the linear part of the sigmoid were retained for a linear regression analysis and used to estimate the inhibitory concentration IC_{50}. The products are solubilized in dimethylsulphoxide (DMSO) at 10^{-2} M and finally used in culture with 0.1% DMSO.

Results of the tests

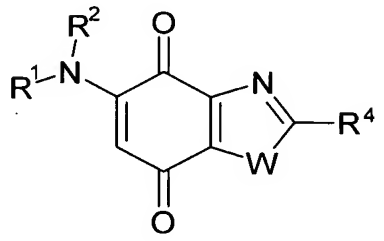
a) The compounds of Examples 1 to 7 have an IC_{50} less than or equal to 10 µM on the phosphatase activity of the purified Cdc25-C recombinant enzyme.

b) The compounds of Examples 1 to 7 have an IC_{50} less than or equal to 10 μM on the cell proliferation of the Mia-Paca2 lines.

c) The compounds of Examples 1 to 7 have a IC_{50} less than or equal to 10 μM on the cell proliferation of the DU-145 lines.

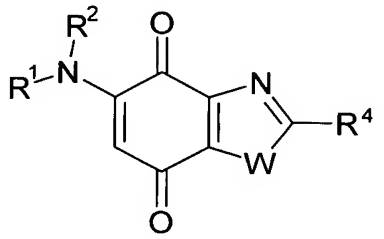
Claims

1. Process for the preparation of a compound of general formula $(I)_1$



$(I)_1$

or of a compound of general formula $(I)_2$



$(I)_2$

in which:

W represents a sulphur atom in general formula $(I)_1$ and an oxygen atom in general formula $(I)_2$,

R^1 represents a hydrogen atom or an alkyl, alkoxyalkyl, alkylthioalkyl, cycloalkyl, $-(CH_2)-X-Y$, $-(CH_2)-Z-NR^5R^6$ radical or a $-CHR^{35}R^{36}$ radical in which R^{35} and R^{36} form together with the carbon atom which carries them an indanyl or tetralinyl radical, or also R^{35} and R^{36} form together with the carbon atom which carries them a saturated heterocycle containing 5 to 7 members and 1 to 2 heteroatoms chosen from O, N and S, the nitrogen atoms of said heterocycle being optionally substituted by radicals chosen from the alkyl radicals and the benzyl radical,

R^1 also being able, when W represents O, to represent moreover a carbocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl or alkoxy radical,

X representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

Y representing a saturated carbon-containing cyclic system containing 1 to 3 condensed rings chosen independently from rings with 3 to 7 members, or Y representing a saturated heterocycle containing 1 to 2 heteroatoms chosen independently from O, N and S and attached to the X radical by an N or CH member, said saturated heterocycle containing moreover 2 to 6 additional members chosen independently from -CHR^7-, -CO-, -NR^8-, -O- and -S-, R^7 representing a hydrogen atom or an alkyl radical and R^8 representing a hydrogen atom or an alkyl or aralkyl radical, or also Y representing a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^9 radical and an $NR^{10}R^{11}$ radical, R^9 representing a hydrogen atom or an alkyl or phenyl radical, and R^{10} and R^{11} independently representing alkyl radicals,

Z representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

R^5 and R^6 being chosen independently from a hydrogen atom, an alkyl, aralkyl or -$(CH_2)_n$-OH radical in which n represents an integer from 1 to 6,

or R^5 representing an alkoxycarbonyl, haloalkoxycarbonyl or aralkoxycarbonyl radical and R^6 representing a hydrogen atom or a methyl radical,

or also R^5 and R^6 forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the –$CR^{12}R^{13}$-, -O-, -S- and -NR^{14}- radicals, R^{12} and R^{13} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{14} representing a hydrogen atom or an alkyl or aralkyl radical, or also R^{14} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^2 representing a hydrogen atom or an alkyl or aralkyl radical;

or also R^1 and R^2 forming together with the nitrogen atom a heterocycle with 4 to 8 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the -$CR^{15}R^{16}$-, -O-, -S- and -NR^{17}- radicals, R^{15} and R^{16} independently representing each time that they occur a

hydrogen atom or an alkyl radical, and R^{17} representing a hydrogen atom or an alkyl or aralkyl radical; and

R^4 represents an alkyl, cycloalkyl, cycloalkylalkyl, cyano, amino, $-CH_2-COOR^{18}$, $-CH_2-CO-NR^{19}R^{20}$ or $-CH_2-NR^{21}R^{22}$ radical, or R^4 represents a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy, haloalkoxy or $NR^{37}R^{38}$ radical, or also R^4 represents a phenyl radical possessing two substituents which form together a methylenedioxy or ethylenedioxy radical,

R^{18} representing a hydrogen atom or an alkyl radical,

R^{19} representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^{23} radical and an $NR^{24}R^{25}$ radical, R^{23} representing a hydrogen atom or an alkyl or phenyl radical, and R^{24} and R^{25} independently representing alkyl radicals,

R^{20} representing a hydrogen atom or an alkyl radical,

or also R^{19} and R^{20} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{26}R^{27}-$, -O-, -S- and $-NR^{28}-$ radicals, R^{26} and R^{27} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{28} representing a hydrogen atom or an alkyl or aralkyl radical, or also R^{28} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{21} representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^{29} radical and an $NR^{30}R^{31}$ radical, R^{29} representing a hydrogen atom or an alkyl or phenyl radical, and R^{30} and R^{31} independently representing alkyl radicals,

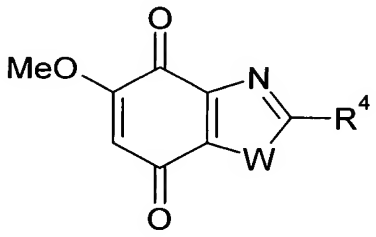
R^{22} representing a hydrogen atom or an alkyl radical,

or also R^{21} and R^{22} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{32}R^{33}-$, -O-, -S- and $-NR^{34}-$ radicals, R^{32} and R^{33} independently representing each time that they occur a

hydrogen atom or an alkyl radical, and R^{34} representing a hydrogen atom, an alkyl or aralkyl radical, or also R^{34} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{37} and R^{38} being chosen independently from a hydrogen atom and an alkyl radical or R^{37} and R^{38} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{39}R^{40}-$, -O-, -S- and $-NR^{41}-$ radicals, R^{39} and R^{40} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{41} representing a hydrogen atom or an alkyl radical,

said process being characterized in that the compound of general formula **(A)**



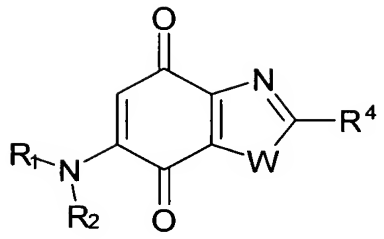
(A)

in which W represents a sulphur atom or an oxygen atom and R^4 has the same meaning as in general formula $(I)_1$ or $(I)_2$ is reacted with an amine of general formula R^1R^2NH in a protic solvent.

2. Process according to claim 1, characterized in that the compound of general formula $(I)_1$ or $(I)_2$ is such that:

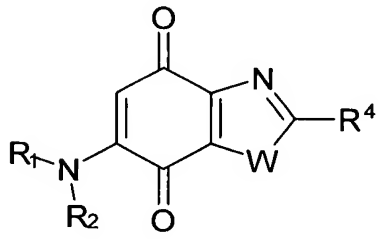
- R^1 represents a $-(CH_2)-Z-NR^5R^6$ radical;
- R^2 represents a hydrogen atom; and
- R^4 represents an alkyl radical or also a phenyl, pyridyl, thienyl or furanyl radical optionally substituted by 1 to 4 halogen atoms or by an $NR^{37}R^{38}$ radical.

3. Process for the preparation of a compound of general formula $(I)_3$



(I)$_3$

or of a compound of general formula **(I)$_4$**



(I)$_4$

in which:

W represents a sulphur atom in general formula **(I)$_3$** and an oxygen atom in general formula **(I)$_4$**,

R^1 represents a hydrogen atom or an alkyl, alkoxyalkyl, alkylthioalkyl, cycloalkyl, -(CH_2)-X-Y, -(CH_2)-Z-NR^5R^6 radical or a -$CHR^{35}R^{36}$ radical in which R^{35} and R^{36} form together with the carbon atom which carries them an indanyl or tetralinyl radical, or also R^{35} and R^{36} form together with the carbon atom which carries them a saturated heterocycle containing 5 to 7 members and 1 to 2 heteroatoms chosen from O, N and S, the nitrogen atoms of said heterocycle being optionally substituted by radicals chosen from the alkyl radicals and the benzyl radical,

R^1 also being able, when W represents O, to represent moreover a carbocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl or alkoxy radical,

X representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

Y representing a saturated carbon-containing cyclic system containing 1 to 3 condensed rings chosen independently from rings with 3 to 7 members, or Y representing a saturated heterocycle containing 1 to 2 heteroatoms chosen independently from O, N and S and attached to the X radical by an N or CH member, said saturated heterocycle

containing moreover 2 to 6 additional members chosen independently from -CHR^7-, -CO-, -NR^8-, -O- and -S-, R^7 representing a hydrogen atom or an alkyl radical and R^8 representing a hydrogen atom or an alkyl or aralkyl radical, or also Y representing a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^9 radical and an $NR^{10}R^{11}$ radical, R^9 representing a hydrogen atom or an alkyl or phenyl radical, and R^{10} and R^{11} independently representing alkyl radicals,

Z representing a bond or a linear or branched alkylene radical containing 1 to 5 carbon atoms,

R^5 and R^6 being chosen independently from a hydrogen atom, an alkyl, aralkyl or $-(CH_2)_n$-OH radical in which n represents an integer from 1 to 6,

or R^5 representing an alkoxycarbonyl, haloalkoxycarbonyl or aralkoxycarbonyl radical and R^6 representing a hydrogen atom or a methyl radical,

or also R^5 and R^6 forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{12}R^{13}$-, -O-, -S- and -NR^{14}- radicals, R^{12} and R^{13} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{14} representing a hydrogen atom or an alkyl or aralkyl radical, or also R^{14} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^2 representing a hydrogen atom or an alkyl or aralkyl radical;

or also R^1 and R^2 forming together with the nitrogen atom a heterocycle with 4 to 8 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the -$CR^{15}R^{16}$-, -O-, -S- and -NR^{17}- radicals, R^{15} and R^{16} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{17} representing a hydrogen atom or an alkyl or aralkyl radical; and

R^4 represents an alkyl, cycloalkyl, cycloalkylalkyl, cyano, amino, $-CH_2-COOR^{18}$, $-CH_2-CO-NR^{19}R^{20}$ or $-CH_2-NR^{21}R^{22}$ radical, or R^4 represents a carbocyclic or heterocyclic aryl radical optionally substituted 1 to 4 times by substituents chosen independently from a halogen atom and an alkyl, haloalkyl, alkoxy, haloalkoxy or $NR^{37}R^{38}$ radical, or also R^4 represents a phenyl radical possessing two substituents which form together a methylenedioxy or ethylenedioxy radical,

R^{18} representing a hydrogen atom or an alkyl radical,

R^{19} representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^{23} radical and an $NR^{24}R^{25}$ radical, R^{23} representing a hydrogen atom or an alkyl or phenyl radical, and R^{24} and R^{25} independently representing alkyl radicals,

R^{20} representing a hydrogen atom or an alkyl radical,

or also R^{19} and R^{20} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{26}R^{27}-$, -O-, -S- and $-NR^{28}-$ radicals, R^{26} and R^{27} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{28} representing a hydrogen atom or an alkyl or aralkyl radical, or also R^{28} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{21} representing a hydrogen atom, an alkyl radical or an aralkyl radical the aryl group of which is optionally substituted 1 to 3 times by substituents chosen independently from the group constituted by a halogen atom, an alkyl radical, a haloalkyl radical, an alkoxy radical, a haloalkoxy radical, a hydroxy radical, a nitro radical, a cyano radical, the phenyl radical, an SO_2NHR^{29} radical and an $NR^{30}R^{31}$ radical, R^{29} representing a hydrogen atom or an alkyl or phenyl radical, and R^{30} and R^{31} independently representing alkyl radicals,

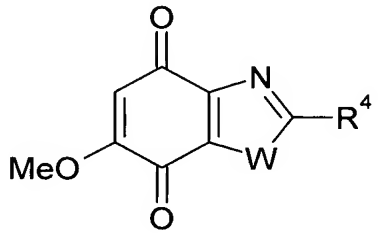
R^{22} representing a hydrogen atom or an alkyl radical,

or also R^{21} and R^{22} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{32}R^{33}-$, -O-, -S- and $-NR^{34}-$ radicals, R^{32} and R^{33} independently representing each time that they occur a hydrogen atom or an alkyl radical, and R^{34} representing a hydrogen atom, an alkyl or aralkyl radical, or also R^{34} representing a phenyl radical optionally substituted 1 to 3 times by substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{37} and R^{38} being chosen independently from a hydrogen atom and an alkyl radical or R^{37} and R^{38} forming together with the nitrogen atom a heterocycle with 4 to 7 members comprising 1 to 2 heteroatoms, the members necessary to complete the heterocycle being chosen independently from the $-CR^{39}R^{40}-$, -O-, -S- and $-NR^{41}-$ radicals, R^{39} and R^{40} independently representing each time that they occur a

hydrogen atom or an alkyl radical, and R^{41} representing a hydrogen atom or an alkyl radical;

said process being characterized in that the compound of general formula **(K)**



(K)

in which W represents a sulphur atom or an oxygen atom and R^4 has the same meaning as in general formula $(I)_3$ or $(I)_4$ is reacted with an amine of general formula R^1R^2NH in a protic solvent.

4. Process according to claim 3, characterized in that the compound of general formula $(I)_3$ or $(I)_4$ is such that:

- R^1 represents a $-(CH_2)-Z-NR^5R^6$ radical;
- R^2 represents a hydrogen atom; and
- R^4 represents an alkyl radical or also a phenyl, pyridyl, thienyl or furanyl radical optionally substituted by 1 to 4 halogen atoms or by an $NR^{37}R^{38}$ radical

5. Compound of the general formulae $(I)_1$ as defined in claim 1 chosen from the following compounds:

- 2-(2,6-difluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione;

- 2-(2,5-dichlorothien-3-yl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione;

- 2-(2,5-dichlorothien-3-yl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione;

- 5-{[2-(dimethylamino)ethyl]amino}-2-(4-fluorophenyl)-1,3-benzothiazole-4,7-dione;

- 2-(4-fluorophenyl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione;

- 2-(2-chloro-6-fluorophenyl)-5-{[2-(dimethylamino)ethyl]amino}-1,3-benzothiazole-4,7-dione;

- 2-(2-chloro-6-fluorophenyl)-5-[(2-pyrrolidin-1-ylethyl)amino]-1,3-benzothiazole-4,7-dione;

or a salt of one of the latter.

6. As a medicament, a compound chosen from the compounds of claim 7, or a pharmaceutically acceptable salt of one of these compounds.

7. Use of a compound according to claim 5, or of a pharmaceutically acceptable salt of one of these compounds, for preparing a medicament intended to treat cancer.

8. Use according to claim 7, characterized in that the cancer is chosen from breast cancer, lymphomas, cancers of the neck and head, lung cancer, cancer of the colon, prostate cancer and cancer of the pancreas.

9. As a novel industrial product, a compound of general formula **(A)** as defined in claim 1,

it being understood however that if W represents a sulphur atom then R^4 is not methyl,

or a salt of the latter.

10. As a novel industrial product, a compound of general formula **(K)** as defined in claim 3,

it being understood however that if W represents a sulphur atom then R^4 is not the phenyl group,

or a salt of the latter.

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PATENT OF INVENTION
Utility certificate
Intellectual property code – Book VI

cerfa No 11235 02

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7500 Paris Cedex 08
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Designation of inventor(s) Page no. 1/2
(If the applicant is not the inventor or the sole inventor)

This form must be completed clearly in black ink

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Your references for this file *(optional)*	RS 337 – ER/MM
National registration no.	0307648

Title of the invention (200 characters or spaces maximum)

Benzothiazole-4,7-diones and benzooxazole-4,7-diones substituted in position 5 or 6 and processes for their preparation

Applicant(s):
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DATE AND SIGNATURE(S) OF APPLICANT(S) OR REPRESENTATIVE (Name and capacity of signatory)
Paris, 16th June 2003

André BOURGOUIN, Representative

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